



SEQUENCE LISTING

- <110> Lane, David
 Bottger, Volker
 Bottger, Angelica
 Picksley, Stephen
 Chene, Patrick
 Hochkeppel, Heinz-Kurt
 Garcia-Echeverria, Carlos
 Furet, Pascal

 <120> Inhibitors of the Interaction of P53 and MDM2

 <130> 4-20937/A/PCT

 <140> herewith

 <141> 1999-01-05

 <150> PCT/EP97/03549

 <151> 1997-07-04

 <160> 83

 <170> PatentIn Ver. 2.0

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Beta C1 cont

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Pro Leu Ser Gln Gln Thr Phe Ser Asp Leu Trp Lys Leu Leu Pro Glu
□
1 5 10 15
□
□
Asn Asn Val
□
□
□
□
<210> 2
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<211> 5
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<223> Description of Artificial Sequence:peptide
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□
<220>
□
<223> Where Xaa may be any amino acid
□
□
<400> 2
□
Phe Xaa Xaa Leu Trp
□
1 5
□
□

*Sub C
cont*

□
<210> 3
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<223> Description of Artificial Sequence:peptide
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□
<220>
□
<223> Xaa represents any amino acid and proline,
□ phenylalanine, aspartic acid, tyrosine ,
□ tryptophan and leucine are L-amino acids
□

□
<220>
□

□
<400> 3
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Pro Xaa Phe Xaa Asp Tyr Trp Xaa Xaa Leu
□
1 5 10
□

□
.

□
<210> 4
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*B I
Cont*

<220>
 <221> VARIANT
 <222> (1) ...
 <223> x=proline, leucine, glutamic acid, cysteine or
 glutamine

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 <221> VARIANT
 <222> (5)
 <223> x = arginine, histidine, glutamic acid, cysteine,
 serine or preferably aspartic acid.

 <220>
 <221> VARIANT
 <222> (6)
 <223> x = histidine, phenylalanine, or preferably
 tyrosine

 <220>
 <221> VARIANT
 <222> (1)
 <223> x=proline, leucine, glutamic acid, cysteine or
 glutamine

 <220>
 <223> Xaa at position 2, 5, 8 and 9 is any amino acid

*Sub C
cont*

B1

cont.

<400> 4
□
Xaa Xaa Phe Xaa Xaa Xaa Trp Xaa Xaa Xaa
□
1 5 10
□
□
□
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<223> Description of Artificial Sequence:peptide
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<222> (1)
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<223> x = proline, leucine, glutamic acid, cysteine or
□
glutamine
□
□
<220>
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<221> VARIANT
□
<222> (2)
□
<223> x = arginine, asparagine, alanine, threonine or
□
valine
□
□
<220>
□
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<222> (4)
□

*Sub C
cont*

*B /
Cont*

<223> X = methionine, isoleucine, threonine, arginine,
 alanine or serine

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<222> (5)

<223> X= arginine, histidine, glutamic acid, cysteine,
 serine or preferably aspartic acid.

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<222> (6)

<223> X = histidine, phenylalanine or preferably
 tyrosine

<220>
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<222> (8) .

<223> X = glutamic acid, threonine, alanine,
 phenylalanine or serine

<220>
 <221> VARIANT

<222> (9)

<223> X= glycine, glutamine, threonine, alanine or
 aspartic acid

<220>

B /
Cont

Sub
C /
Cont

~~<221> VARIANT~~
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~~<222> (10)~~
□
~~<223> Xaa = phenylalanine, glutamine or preferably~~
□
leucine
□

□
<400> 5
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1 5 10
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□
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B¹
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1 5 10
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Sub C¹
Cont.
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B /

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Gln Pro Thr Phe Ser Asp Tyr Trp Lys Leu Leu Pro
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1 5 10
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□

□
<210> 8
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Cont

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Pro Arg Pro Ala Leu Val Phe Ala Asp Tyr Trp Glu Thr Leu Tyr
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1 5 10 15
□

Sub C Cont

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Met Pro Arg Phe Met Asp Tyr Trp Glu Gly Leu Asn Arg Gln Ile Lys
 1 5 10 15

 Ile Trp Phe Gln Asn Arg Arg Met Lys Trp Lys Lys
 20 25

 <210> 10

 <211> 8

 <212> PRT

 <213> Artificial Sequence

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 <223> Description of Artificial Sequence:peptide

B1
Cont.

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 <223> X = methionine, isoleucine, threonine, arginine,
 alanine or serine, preferably methionine

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 <222> (3)

 <223> X = arginine, histidine, glutamic acid, cysteine,
 serine, or preferably aspartic acid.

*Sub C
cont*

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 <221> VARIANT
 <222> (4)
 <223> X = histidine, phenylalanine, or preferably
tyrosine

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 <221> VARIANT
 <222> (6)
 <223> X = glutamic acid, threonine, alanine,
phenylalanine or serine, preferably glutamic acid

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 <221> VARIANT
 <222> (7)
 <223> X = glycine, glutamine, threonine, alanine or
aspartic acid, preferably glycine.

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 <221> VARIANT
 <222> (8)
 <223> X = phenylalanine, glutamine or preferably
leucine.

 <400> 10
 Phe Xaa Xaa Xaa Trp Xaa Xaa Xaa
 1 5

B1
Cont

Sub
C1
Cont

<210> 11

 <211> 9

 <212> PRT

 <213> Artificial Sequence

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 <221> VARIANT

 <222> (1)

 <223> X = arginine, asparagine, alanine, threonine or

valine, particularly arginine.

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 <222> (3)

 <223> X = methionine, isoleucine, threonine, arginine,

alanine or serine, preferably methionine

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 <221> VARIANT

 <222> (4)

 <223> X = arginine, histidine, glutamic acid, cysteine,

serine or preferably aspartic acid.

B1
Cont.

Sub
C1
Cont.

B1
Cont.

<220>
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<222> (5)
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<223> Xaa = histidine, phenylalanine or preferably
□
tyrosine.
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<222> (7)
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<223> X = glutamic acid, threonine, alanine,
□
phenylalanine or serine, preferably glutamic acid.
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<223> X = glycine, glutamine, threonine, alanine or
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aspartic acid preferably glycine.
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<222> (9)
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<223> X = phenylalanine, glutamine or preferably
□
leucine.
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□
<400> 11
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Xaa Phe Xaa Xaa Xaa Trp Xaa Xaa Xaa
□
1 5
□

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Pro Ala Phe Thr His Tyr Trp Pro
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1 5
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<400> 13
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Pro Thr Phe Ser Asp Tyr Trp Pro
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1 5
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□
<210> 14
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*Sub
C
cont*

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<400> 14
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Pro Arg Phe Met Asp Tyr Trp Pro
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1 5
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<210> 15
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Arg Phe Met Asp Tyr Trp Glu Gly Leu
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1 5
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<210> 16
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Sub C¹ cont.

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<400> 16

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Phe Met Asp Tyr Trp Glu Gly Leu

□

1

5

□

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<210> 17

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<213> Artificial Sequence

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<220>

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<223> Description of Artificial Sequence:peptide

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<400> 17

□

Gln Glu Thr Phe Ser Asp Leu Trp Lys Leu Leu Pro

□

1

5

10

□

□

<210> 18

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<211> 12

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<212> PRT

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<213> Artificial Sequence

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*Sub C1
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<21> VARIANT
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<22> (1)
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<23> x = Ac-Thr
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<21> VARIANT
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<22> (12)
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<23> X = Phe-NH2
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<400> 18
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Xaa Gly Pro Ala Phe Thr His Tyr Trp Ala Thr Xaa
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1 5 10
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<210> 19
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<211> 12
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<23> Description of Artificial Sequence:peptide
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<220>
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<21> VARIANT
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C'x
Conf

<222> (1)
□
<223> X = Ac-Met
□
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<220>
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<221> VARIANT
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<222> (12)
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<223> X = Asn-NH2
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<400> 19
□
Xaa Pro Arg Phe Met Asp Tyr Trp Glu Gly Leu Xaa
□
1 5 10
□
□
□
<210> 20
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<211> 12
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<212> PRT
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<221> VARIANT
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<222> (1)
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<223> X = Ac-Gln
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C
Cont*

*Sue
C
Cont*

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<223> Pro-NH₂
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1 5 10
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□

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<210> 21
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<222> (1)
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<223> X = Ac-Pro
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<222> (8)
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<223> X = Pro-NH₂
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<210> 22

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<223> X = Ac-Pro

<220>

<221> VARIANT

<222> (8)

<223> X = Pro-NH₂

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Xaa Thr Phe Ser Asp Tyr Trp Xaa

1 5

<210> 23

<211> 8

*Sue
C &
Cont*

<212> PRT
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<222> (1)
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<223> X = Ac-Pro
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<222> (8)
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<223> X = Pro-NH2
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<400> 23
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Xaa Arg Phe Met Asp Tyr Trp Xaa
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5

Sab C1 Ami
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<210> 24
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<222> (1)
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<223> X = Ac-Gln
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<221> VARIANT
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<222> (12)
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<223> X = Pro-NH2
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<220>
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<223> Description of Artificial Sequence:peptide
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<400> 24
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Xaa Glu Thr Phe Ser Asp Leu Trp Lys Leu Leu Xaa
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1 5 10
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<210> 25
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<223> Ac-Gln
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*Sub
C^t
cent*

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 <222> (12)
 <223> X = Pro-NH₂

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Xaa Pro Thr Phe Ser Asp Leu Trp Lys Leu Leu Xaa

1 5 10

<210> 26
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 <223> X = Ac-Gln

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 <221> VARIANT
 <222> (12)
 <223> X = Pro-NH₂

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Xaa Glu Thr Phe Ser Asp Tyr Trp Lys Leu Leu Xaa
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1 5 10
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□
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<210> 27
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<211> 12
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<212> PRT
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<223> Description of Artificial Sequence:peptide
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<222> (1)
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<223> X = Ac-Val
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<220>
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<222> (12)
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<223> X=Phe-NH2
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1 5 10
□

□
<210> 28
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<211> 15
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<213> Artificial Sequence
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<220>
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<223> Description of Artificial Sequence:peptide
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<223> X = Ac-Ile
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<223> X = Val-NH2
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Xaa Asp Arg Ala Pro Thr Phe Arg Asp His Trp Phe Ala Leu Glx
□
 1 5 10 15
□

□

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<210> 29
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<222> (1)
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<223> X = Ac-Pro
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<223> X = Tyr-NH2
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1 5 10 15
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<223> X = Ac-Pro
□

□
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<222> (15)
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<223> X = His-NH2
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Xaa Ala Phe Ser Arg Phe Trp Ser Asp Leu Ser Ala Gly Ala Xaa
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1 5 10 15
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<210> 31
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<223> X = Phe-NH2
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□
<400> 31
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Thr Gly Pro Ala Phe Thr His Tyr Trp Ala Thr Xaa

□

1

5

10

□

□

□

<210> 32

□

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□

<212> PRT

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<213> Artificial Sequence

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<220>

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<223> Description of Artificial Sequence:peptide

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<220>

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<221> VARIANT

□

<222> (12)

□

<223> X = Asn-NH2

□

□

<400> 32

□

Met Pro Arg Phe Met Asp Tyr Trp Glu Gly Leu Xaa

□

1

5

10

□

□

<210> 33

□

<211> 14

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□
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□
<223> X = Ac-Cys(Acrlid) or Ac-Cys
□

□
<220>
□
<221> VARIANT
□
<222> (14)
□
<223> X = Pro-NH₂ .
□

□
<400> 33
□
Xaa Gly Gln Pro Thr Phe Ser Asp Tyr Trp Lys Leu Leu Xaa
□
1 5 10
□

□
<210> 34
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<211> 14
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<212> PRT
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<213> Artificial Sequence
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<220>
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<223> Description of Artificial Sequence:peptide
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<220>
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<223> X = Pro-NH2
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□
<220>
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<221> UNSURE
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<222> (1)
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<223> X = Ac-Cys
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Xaa Gly Gln Pro Thr Phe Ser Asp Tyr Trp Lys Leu Leu Xaa
□
1 5 10
□
□
□
<210> 35
□
<211> 10
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<223> Description of Artificial Sequence:peptide
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□
<220>
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<221> VARIANT
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<222> (1)
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<223> X = Ac-Cys (Acrd)
□
□
<220>
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<221> VARIANT
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<222> (10)
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<223> X = Pro-NH2

□

□

<400> 35

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Xaa Gly Pro Thr Phe Ser Asp Leu Trp Xaa

□

1

5

10

□

□

<210> 36

□

<211> 10

□

<212> PRT

□

<213> Artificial Sequence

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<220>

□

<223> Description of Artificial Sequence:peptide

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□

<220>

□

<221> VARIANT

□

<222> (1)

□

<223> X = Ac-Cys

□

□

<220>

□

<221> VARIANT

□

<222> (10)

□

<223> x = Pro-NH2

□

□

<400> 36

□

Xaa Gly Pro Thr Phe Ser Asp Leu Trp Xaa

□

1

5

10

□

□
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<210> 37
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□
<223> Description of Artificial Sequence:peptide
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<220>
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<222> (1)
□
<223> X = Ac=Cys(Acrd)
□

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<221> VARIANT
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<222> (9)
□
<223> X = Pro-NH2
□

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Xaa Pro Thr Phe Ser Asp Leu Trp Xaa
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 1 5
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<213> Artificial Sequence
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<223> X = Pro-NH2
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Xaa Pro Thr Phe Ser Asp Leu Trp Xaa
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 1 5
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□
<210> 39
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<211> 16
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1 5 10 15
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<210> 40
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1 5 10 15
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<210> 41
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<400> 41
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1 5 10 15
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<210> 42
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<211> 29
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<400> 42
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Xaa Met Pro Arg Phe Met Asp Tyr Trp Glu Gly Leu Asn Arg Gln Ile
□
1 5 10 15
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Lys Ile Trp Phe Gln Asn Arg Arg Met Lys Trp Lys Xaa
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20

25

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□

<210> 43

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<211> 16

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<212> PRT

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<400> 43

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Arg Gln Ile Lys Ile Trp Phe Gln Asn Arg Arg Met Lys Trp Lys Lys

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<210> 44

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<211> 31

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<223> product = bAla
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Xaa Ala Val Ala Leu Leu Pro Ala Val Leu Leu Ala Leu Leu Ala Pro
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 1 5 10 15

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Ala Met Pro Arg Phe Met Asp Tyr Trp Glu Gly Leu Asn Ala Xaa
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 20 25 30

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<400> 45
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1 5 10 15
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<210> 46
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<211> 8
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<223> X = Cys-NH2
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Xaa Thr Phe Ser Asp Tyr Trp Xaa

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<210> 47

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<211> 8

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<212> PRT

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<213> Artificial Sequence

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<223> Description of Artificial Sequence:peptide

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<220>

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<222> (1)

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<223> X = Ac-Cys

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<221> VARIANT

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<222> (8)

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<223> X = Cys-NH2

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□

<400> 47

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Xaa Thr Phe Ser Asp Tyr Trp Xaa

□ 1 5

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□

<210> 48

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<211> 8
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<222> (8)
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<223> X = Cys-NH2
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<400> 48
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Xaa Ala Phe Thr His Tyr Trp Xaa
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1 5
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□
<210> 49
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<211> 8
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<212> PRT
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<223> Description of Artificial Sequence:peptide
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<223> X = Cys-NH2
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<400> 49
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Xaa Ala Phe Thr His Tyr Trp Xaa
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1 5
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□

□
<210> 50
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<211> 8
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<212> PRT
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<223> x = Ac-Cys
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<222> (8)
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<223> X = Cys-NH2
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<400> 50
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Xaa Arg Phe Met Asp Tyr Trp Xaa
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1 5
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□

□
<210> 51
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<211> 8
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<223> X = Cys-NH2

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<400> 51

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Xaa Arg Phe Met Asp Tyr Trp Xaa

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1

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□

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<210> 52

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<211> 8

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<212> PRT

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<213> Artificial Sequence

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<220>

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<223> Description of Artificial Sequence:peptide

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<220>

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<221> VARIANT

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<222> (1)

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<223> X = Ac-Glu

□

□

<220>

□

<221> VARIANT

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<222> (8)

□

<223> X = Lys-NH2

□

□

<400> 52

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Xaa Thr Phe Ser Asp Tyr Trp Xaa

□

1

5

□

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<210> 53
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<220>
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<223> X = CO-NH bridge (lactam peptide derivative)
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<222> (1)
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<223> X = Ac-Glu
□

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<223> X = CO-NH bridge (lactam peptide derivative)
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<223> X = Lys-NH₂
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<400> 53
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Xaa Arg Phe Met Asp Tyr Trp Xaa
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1 5
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<210> 54
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<223> Product = Aib
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<223> Product = Aib

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<222> (8)

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<223> X = Leu-NH2

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□

<400> 54

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Xaa Met Xaa Tyr Trp Xaa Gly Xaa

□

1

5

□

□

<210> 55

□

<211> 9

□

<212> PRT

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<213> Artificial Sequence

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<223> Description of Artificial Sequence:peptide

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<221> VARIANT

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<222> (1)

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<223> X = Ac-Arg

□

□

<220>

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<222> (4)

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Xaa Phe Met Xaa Tyr Trp Xaa Gly Xaa
□
 1 5
□

□
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<223> X = Ac3c

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<223> X = Leu-NH2

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□

<400> 56

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Xaa Phe Met Xaa Tyr Trp Glu Xaa Xaa

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1

5

□

□

<210> 57

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<211> 8

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<223> Product = Aib

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<222> (6)

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<223> Product = Aib

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□

<220>

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<222> (7)

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<223> X = Ac3c

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□

<220>

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<221> VARIANT

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<222> (8)

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<223> X = Leu-NH2

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<400> 57

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Xaa Met Xaa Tyr Trp Xaa Xaa Xaa
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□ 1 □ 5
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<222> (7)
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<223> x = Ac3c
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<223> x = Leu-NH2
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Xaa Met Xaa Tyr Trp Gln Xaa Xaa
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<223> X = Leu-NH2
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<210> 60
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<223> x = Leu-NH2
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<211> 8
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<223> product = Aib
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<223> x = Leu-NH2
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Xaa Met Xaa Tyr Trp Glu Gly Xaa
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1 5
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<211> 8
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<222> (6)
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<223> Product = Aib
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<221> VARIANT
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<222> (8)
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<223> X = Leu-NH2
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Xaa Met Asp Tyr Trp Xaa Gly Xaa
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1 5
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<210> 63
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<211> 12
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Val Gln Asn Phe Ile Asp Tyr Trp Thr Gln Gln Phe
□
1 5 10
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□

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<210> 64
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<211> 12
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Thr Gly Pro Ala Phe Thr His Tyr Trp Ala Thr Phe
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1 5 10
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□

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<213> Artificial Sequence

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<220>

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<223> Description of Artificial Sequence:peptide

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<400> 65

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Ile Asp Arg Ala Pro Thr Phe Arg Asp His Trp Phe Ala Leu

□

1

5

10

□

□

<210> 66

□

<211> 15

□

<212> PRT

□

<213> Artificial Sequence

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<220>

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<223> Description of Artificial Sequence:peptide

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□

<400> 66

□

Pro Ala Phe Ser Arg Phe Trp Ser Asp Leu Ser Ala Gly Ala His

□

1

5

10

15

□

□

<210> 67

□

<211> 30

□

<212> DNA

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<213> Artificial Sequence

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<220>
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gcggatccga tggtagggag caggcaaatg . 30
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<210> 68
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<211> 33
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<212> DNA
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<400> 68
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gcctgcagcc taattcgatg gcgtccctgt aga . 33
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<210> 69
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<211> 32
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<212> DNA
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<223> Description of Artificial Sequence:primer DNA
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<400> 69
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gcctgcagct agggaaata agttagcaca at . 32
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<210> 70
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<211> 32
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<212> DNA
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<400> 70
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gcctgcagct aatcttcttc aaatgaatct gt 32
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<210> 71
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<211> 27
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<400> 71
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ggggatcctg aaatttcctt agctgac 27
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<210> 72
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<211> 29
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<212> DNA
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<213> Artificial Sequence
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<220>
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<223> Description of Artificial Sequence:primer DNA

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<400> 72

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gcggatccat ggtgaggagc aggcaaatg

29

□

<210> 73

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<211> 22

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<212> PRT

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<213> Artificial Sequence

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<220>

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<223> Description of Artificial Sequence:peptide

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□

<220>

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<221> VARIANT

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<222> (1)

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<223> X = Biotin-Ser

□

□

<400> 73

□

Xaa Gly Ser Gly Glu Pro Pro Leu Ser Gln Glu Thr Phe Ser Asp Leu

□

1

5

10

15

□

□

Trp Lys Leu Leu Pro Glu

□

20

□

□

<210> 74

□

<211> 18

□

<212> PRT
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<213> Artificial Sequence
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<400> 74
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Pro Pro Leu Ser Gln Glu Thr Phe Ser Asp Leu Trp Lys Leu Leu Pro
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□

□
Glu Asn
□

□

□
<210> 75
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<211> 57
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<212> DNA
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<213> Artificial Sequence
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gtccgcctct gagtcaggaa acatttcag acctatggaa actacttcct gaaaacg 57
□

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<210> 76
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<211> 58
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<212> DNA
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<213> Artificial Sequence
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<400> 76
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gtccgcctct gagtcaggaa acatttcag acctatggaa actacttcct gaaaacg 57
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□
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Thr Phe Ser Asp Leu Trp

□

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5

B
Gut
Sub
C'
cont'